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Pediatrics and Neonatology (2017) xx, 1-5



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Original Article

Urinary tract infections in neonates with unexplained pathological indirect hyperbilirubinemia: Prevalence and significance

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Received Jan 30, 2017; received in revised form Aug 14, 2017; accepted Oct 25, 2017 Available online ■ ■ ■

Key Words

follow-up; hyperbilirubinemia; neonate; urinary tract infection; prevalence Abstract Background: It is controversial to test for urinary tract infection (UTI) in patients with unexplained indirect hyperbilirubinemia in the first 2 weeks of life. We aimed to study the prevalence and significance of UTIs in such neonates who were requiring phototherapy. Methods: Subjects were 2- to 14-day-old neonates with indirect bilirubin levels above phototherapy limit with no other abnormality in their bilirubinaemia-related etiologic workup. UTI was diagnosed by 2 consecutive positive cultures obtained by catheterisation, documenting growth of >10,000 colonies of the same microorganism with consistent antibiograms. The UTI (+) patients were evaluated by renal ultrasonography (US), and some were followed up for possible recurrent UTI.

Results: 262 neonates were included in the study. UTI prevalence was 12.2%, and bacteraemia was 6.2% among UTI (+) patients. The two most common pathogens (81.2%) were *Escherichia coli* and *Klebsiella. pneumonia*. All UTI (+) patients had undergone US, revealing 12.5% pelvicaliectasis, other 12.5% increased renal parenchymal echogenicity, 3.1% concurrent pelvicaliectasis and increased renal parenchymal echogenicity. 53.1% of UTI (+) patients had undergone follow-up, after which 23.5% recurrent UTI were found at the end of a mean of 52 months.

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https://doi.org/10.1016/j.pedneo.2017.10.010

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Please cite this article in press as: Bahat Ozdogan E, et al., Urinary tract infections in neonates with unexplained pathological indirect hyperbilirubinemia: Prevalence and significance, Pediatrics and Neonatology (2017), https://doi.org/10.1016/j.pedneo.2017.10.010

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Conclusion: We suggest that the neonates with unexplained pathological jaundice should be tested for possible UTI. Consequently, all newborns with UTI shall be evaluated by the urinary US and followed up for recurrent UTI.

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1. Introduction

Neonatal hyperbilirubinemia is seen in the first week of life in 60% of the term and 80% of the preterm newborns. In these cases, bilirubin levels may remain in the physiologic range or may exceed the level requiring phototherapy or blood exchange. The aetiology of pathologic hyperbilirubinemia could not always be determined.

Urinary tract infection (UTI) presents with variable symptoms in the neonatal period. Nonspecific complaints (i.e., poor weight gain, vomiting, diarrhoea, fever, irritability, lethargy, jaundice) may be the only symptoms, among which jaundice is documented as one of the most common. UTIs are well-known to cause prolonged jaundice and investigated as a standard of care. Along with prolonged jaundice, UTIs may underlie the unexplained pathologic jaundice presenting in the first 2 weeks of life. It is still controversial to test for UTI in patients with unexplained jaundice presenting in the first 2 weeks of life. Hence, some authors suggest investigating these neonates requiring treatment for pathologic indirect hyperbilirubinemia for UTIs, 3,4,6,7,9 while some do not. 5,8

In this report, we aimed to study the prevalence and significance of UTIs in neonates presenting with indirect hyperbilirubinemia in the first 2 weeks of life requiring phototherapy who were found to have no other abnormality in their aetiologic workup.

2. Material and methods

This study was performed between November 2004 and November 2007 in the Karadeniz Technical University Farabi Hospital neonatal intensive care unit, Turkey. Some patients were followed up until December 2013 by the Paediatric Nephrology Department. Subjects were 2- to 14-dayold neonates with indirect bilirubin levels above the phototherapy limit with no other abnormality in their bilirubinaemia-related aetiologic workup for systemic infection, isoimmunisation, erythrocyte enzyme defect, erythrocyte structural defect, hypothyroidism, sequestrated blood, polycythaemia or metabolic disease. Phototherapy limits of bilirubin levels were determined according to the guidelines of American Pediatrics Academy. 10

Method of delivery, sex, birth weight, weight at presentation, gestational age, postnatal age at presentation, weight loss, breast feeding data, onset of jaundice by history, bilirubin level at presentation, duration of phototherapy and requirement of blood exchange were recorded. Tests for blood group, mother's blood group, direct Coombs

test, complete blood count, peripheral blood smear, reticulocyte count, serum total/direct bilirubin, glucose, blood urea nitrogen, creatinine, sodium and urinalysis were performed. If the aetiology of jaundice could not be explained by blood group incompatibility, glucose-6phosphate dehydrogenase and pyruvate kinase enzyme levels, urinary reducing substances, thyroid hormones and urine cultures were analysed. Polycythaemia was defined as the haemoglobin concentration greater than two standard deviations above the normal value for gestational and postnatal age. Urine samples for urinalysis and urine culture were obtained using catheterisation. The samples were analysed with Clinitek 100 (Bayer) or IQ 200 (IRIS) automatic analysers. Pyuria was defined as the presence of >5 leukocytes in one high-power field in the sediment of centrifuged urine. Presence of >1 microorganism in one immersion field by Gram stain was accepted as bacteriuria. In the urinary culture, \geq 10,000 colonies of a single pathogen were regarded as significant.⁶ In patients with a positive urine culture, before initiation of relatedantibiotherapy, blood cultures and confirmatory catheter urine culture were obtained. Immature/total neutrophil ratio was determined using a peripheral blood smear. Creactive protein >5 mg/L and procalcitonin >0.5 μ g/L were regarded as significant. In patients who had elevated acutephase reactant levels or positive blood cultures, lumbar puncture was also performed.

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UTI was diagnosed in patients with confirmatory urine culture >10.000 colonies of the same microorganism with the first culture and related antibiogram. Patients with bilirubin levels above the phototherapy cutoff level and negative cultures were accepted as the UTI (-) group. Patients whose second urine culture was negative, positive for a different organism, or yielded multiple microorganisms or had no parent-given informed were excluded from the study. UTI (+) and (-) patients were compared for the above parameters (i.e., birth weight, gestational age, sex, delivery method, weight at presentation, weight loss, onset of jaundice, time of presentation, total/direct bilirubin at presentation, blood exchange, duration of phototherapy, urine density, presence of hypoglycaemia hypernatraemia).

As secondary analyses, all UTI (+) patients were evaluated by renal ultrasonography (US). All were offered to have voiding cystourethrogram (VCUG) at least 1 month after the sterilisation of urine cultures and dimercaptosuccinic acid scintigraphy (DMSA). Their follow-up data were evaluated.

Informed consent was obtained from the parents of all patients, and the study was approved by the local institutional ethical board (approval number: 200691).

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